The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 50

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte D. CLARK BENNETT,
ELIZABETH CAUCHON, DOMINIQUE FINK,
BRIGETTE GROUIX, ARIANE HSIA,
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U.S. PATENT AND TRADEMARK OFFICE
BOARD OF PATENT APPEALS
AND INTERFERENCES

Appeal No. 2003-1678
Application No. 08/722,659

ON BRIEF

WILLIAM F. SMITH, MILLS, and GREEN, Administrative Patent Judges.

WILLIAM F. SMITH, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision under 35 U.S.C. § 134 from the final rejection of claims 1 through 7, 18, and 19, all the claims remaining in the application. Claim 1 is representative of the subject matter on appeal and reads as follows:

1. A method to decrease localized inflammatory responses arising from an ischemia/reperfusion injury in a tissue of a patient comprising intravascularly administering to said patient heparinase enzyme in an effective amount sufficient to decrease neutrophil transmigration through activated endothelium and basement membrane of said vasculature which decreases said localized inflammatory response arising from an ischemia/reperfusion injury.

The reference relied upon by the examiner is:

Zimmermann et al. (Zimmermann) 5,997,863 Dec. 7, 1999

Claims 1 through 7, 18, and 19 stand rejected under 35 U.S.C. § 102(e) or § 102(f) as anticipated by Zimmermann. We affirm the rejection premised upon 35 U.S.C. § 102(e). Since that constitutes a disposition of the appeal, we need not reach the merits of the alternative rejection under 35 U.S.C. § 102(f).

Background

The invention set forth in the written description of this application is directed to the use of heparinase enzyme to reduce localized inflammatory responses. Specification, page 1. Heparinase acts to degrade heparin and heparan sulfate moieties on the surface of endothelial cells and from basement membranes. Id., page 8. The release of heparin and heparan sulfate moieties in this manner also serves to release chemokines which are bound to the heparin and heparan sulfate. As explained:

> The removal of heparin and heparan sulfate from endothelial cells interferes with L-selectin interactions with endothelium, preventing increased leukocyte rolling. The removal of glycosaminoglycans from endothelial cells and basement membranes also removes glycosaminoglycan bound chemokines, which are critical for leukocyte recruitment. Loss of endothelial cells bound chemokines decreases activation of leukocyte integrins and inhibits firm adhesion by the leukocytes. It also inhibits extravasation of leukocytes, because the leukocytes require the presence of a bound gradient of chemokine for transmigration. It is believed, without being limited, that unbound chemoattractants are depleted from the endothelium layer by blood flow, preventing formation of a significant soluble chemoattractant gradient.
>
> Generally, after a one hour heparinase treatment, 50% of the digested cell surface and basement membrane heparin and heparan

> sulfate are replaced within 2 to 4 hours, and it is completely replaced within 12 to 16 hours. Longer treatment times (3 and 5 hours) greatly extended the time needed to replace the same amount of heparin/ heparan sulfate. Inflammatory responses would be significantly diminished by a slow rate of replacement of cell surface heparin/heparan sulfate. Appropriate administration of heparinase could extend the duration of diminished inflammatory response.

Specification, pages 14 -15.

The claimed invention is directed to decreasing localized inflammatory responses which arise from an ischemia/reperfusion injury in a tissue of a patient. As explained in the specification, ischemia/reperfusion injury can occur from myocardial infarction, shock, stroke, organ transplantation, and cardiopulmonary bypass surgery. Id., page 1. To this end, claim 1 requires that a patient suffering from an ischemia/reperfusion injury be intravascularly administered heparinase enzyme in an "effective amount sufficient to decrease neutrophil transmigration through activated endothelium and basement membrane of said vasculature which decreases said localized inflammatory response arising from an ischemia/reperfusion injury." Examples 5 and 6 of the specification are stated to establish treatment of endothelial cell layers and basement membranes with heparinase serves to inhibit neutrophil extravasation. Examples 7 and 8 of the specification report results obtained from treating rats and rabbits respectively with heparinase following ischemia/reperfusion injury.

Discussion

1. Separate Argument of Claims.

Appellants state "Claims 1-7 and 18-19 stand or fall together." Appeal Brief, page 6. Accordingly, we shall limit our consideration of the issues raised in this appeal

as they apply to claim 1, the only independent claim pending.

2. Procedural Issues.

The Appeal Brief contains Appendices A-G. The examiner stated:

> The papers labeled Appendixes C-G, which are attached to the instant Appeal Brief, will not be considered because there is no showing of good and sufficient reasons why they were not presented earlier. See §1.195 which states 'Affidavits, declarations, or exhibits submitted after the case has been appealed will not be admitted without a showing of good and sufficient reasons why they were not earlier presented.'

Examiner's Answer, page 3. In the Reply Brief, appellants responded to the non-entry of the of Appendices C-G, stating:

> The Examiner has refused to consider Exhibit G of the Appeal Brief and the Singer and Smith review article addressed in Sections A and B of the Appeal Brief. Appellants note that Exhibit G is recent case law regarding anticipation rejections attached for the convenience of the Board. In addition, the Singer and Smith article establishes that inflammation involves the adherence of neutrophils to an activated extracellular matrix followed by the infiltration or transmigration of neutrophils into the wounded area and clearly elucidates the differences between inflammation, tissue formation, and tissue remodeling during the wound healing process. Appellants submit that this Singer and Smith review article was provided with the Response filed March 18, 2002, and should be considered as having been properly before the Examiner during prosecution of the instant application.

Reply Brief, page 4, first full paragraph.

The examiner issued a Communication (Paper No. 48) June 3, 2003, stating the Reply Brief had been entered and considered and the file would be forwarded to the Board for a decision. Thus, as the record now stands, the examiner did not reverse her decision denying entry of Appendices C-G. Accordingly, Appendices C-G are not

before us for review in the considering the issues raised in this appeal.[1]

As a second matter, we note appellants rely upon a declaration filed under 37 CFR § 1.132 of Joseph Zimmermann as well as declarations filed under 37 CFR § 1.132 of Israel Vlodavsky and Richard Brougiton. Reply Brief, page 3. In arguing the rejection premised under 35 U.S.C. § 102(e) on pages 6-13 of the Appeal Brief, appellants did not rely upon any of the three declarations. 37 CFR § 1.192(a) states in relevant part "[a]ny arguments or authorities not included in the brief will be refused consideration by the Board of Patent Appeals and Interferences, unless good cause is shown." Since the three declarations were not relied upon in the Appeal Brief, the arguments set forth in the Reply Brief based upon the three declarations are untimely and improper and will not be considered.

3. Rejection under 35 U.S.C. § 102(e).

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co., 815 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987) (citations omitted). Here, claim 1 requires a single step, i.e., administering intravascularly to a patient heparinase enzyme in a specified "effective amount." The examiner relies upon the procedure set forth in Example 8 of Zimmermann as describing this step.

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[1] Exhibit G is a copy of Elan Pharms., Inc. v. Mayo Found., 304 F.3d 1221, 64 USPQ2d 1292 (Fed. Cir. 2002) (Elan I). The opinion in Elan I has been vacated and replaced. See Elan Pharms., Inc. v. Mayo Found., No. 00-1467 (October 2, 2003) (Elan II). Thus, appellants' reliance upon Elan I is moot.

Example 8 of Zimmermann evaluates the administration of heparinase to a rabbit being used as an ischemic model. Zimmermann states that ischemia was surgically induced in rabbits with heparinase being administered for 10 days beginning on the 11th day following surgery in an amount of 100 IU-day^{-1}. Id., column 17, line 66 - column 18, line 29. The treated rabbits demonstrated increased blood pressure ratio as well as increased revascularization following ischemia. Zimmermann, Table 4. Zimmermann concludes that the data reported in Example 8 indicate the "potential utility" of using heparinase for "accelerating tissue repair in humans."

In determining whether the procedure set forth in Example 8 of Zimmermann meets that required by claim 1 on appeal, the first question is whether the "patient" in Zimmermann is that required by claim 1 on appeal. The "patient" treated in Example 8 Zimmermann was a rabbit. However, Zimmermann indicates the procedure used is a model and that the procedure set forth in the example shows the potential utility of use in humans.

Appellants do not argue that claim 1 differs from the procedure set forth in Example 8 of Zimmermann on the basis of the "patient" being treated. Examples 7 and 8 of this specification also demonstrate the effectiveness of the claimed method using standard laboratory animals, e.g., rats and rabbits. We find no explicit definition of the word "patient" in the written description of this application. Thus, the rabbits treated in Example 8 of Zimmermann with heparinase following surgically induced ischemia are patients within the scope of claim 1 who are suffering from "an ischemia/reperfusion injury."

A second aspect of the single step of claim 1 which needs to be addressed is the requirement that the heparinase be intravascularly administered. Example 8 of Zimmermann does not explicitly state how the heparinase was administered. Given the overall procedure outlined in Example 8 of Zimmermann, it is reasonable to conclude that the heparinase was administered intravascularly. Indeed, Zimmermann describes the administration of heparinase in that invention by means of injection or catheter. Id., column 11, line 61 - column 12, line 3. Again, appellants do not argue this as a point of distinction between the method required by claim 1 on appeal and the method described in Example 8 of Zimmermann.

Since the same "patient" is administered the same active agent, heparinase, by the same mode of administration, intravascularly, the only remaining possible point of distinction is the amount of heparinase administered in the respective methods. As set forth above, Zimmermann administered 100 IU-day^{-1} to the rabbits. Claim 1 on appeal requires a functional amount. Under these circumstances, it is appropriate to review the written description of this application to determine what finite amounts correspond to the functional amount set forth in claim 1 on appeal. In re Woodruff, 919 F.2d 1575, 1577, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990) (It was proper to review Woodruff's specification for disclosed finite times to interpret the claim limitation "for a time sufficient to inhibit the visible birth of fungi."). A review of the specification of this application does not provide much assistance in that it does not set forth specific, finite ranges of heparinase which will result in an "effective amount sufficient to decrease neutrophil transmigration through activated endothelium and basement membrane of

said vasculature which decreases said localized inflammatory response arising from an ischemia/reperfusion injury" as required by claim 1 on appeal. The finite amounts described in the written description of this application are in terms of target dose, e.g., 25 µg/ml, specification, page 40, line 6, or a measured heparinase level in the blood of the laboratory animal, e.g., 1.0 IU/ml (specification, page 37, last full paragraph). It is acknowledged that administering a given active agent in differing amounts may elicit different effects within a defined subset of patients. However, appellants have not argued that the finite amount of heparinase administered to the rabbits in Example 8 of Zimmermann is not a dosage within the functional dosage statement set forth in claim 1 on appeal.

Rather, appellants' argument in this appeal is that Zimmermann does not teach that "heparinase acts to decrease neutrophil transmigration through the activated endothelium and basement membrane." Appeal Brief, page 12. Appellants also argue that Zimmermann teaches heparinase enhances neutrophil transmigration which is contrary to the claimed invention. See, e.g., Appeal Brief, pages 8-9. In essence, appellants' argument is that Zimmermann does not recognize that the induced ischemia of Example 8 resulted in localized inflammation and that the heparinase administered to the rabbits would decrease neutrophil transmigration through activated endothelium and basement membrane which would decrease the local inflammatory response.

However, "[i]t is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable." In re Woodruff, 919 F.2d 1575, 1577, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). Here, appellants'

burden was to distinguish either the patient, active agent, mode of administration, and/or dosage amount required by claim 1 on appeal from those set forth in Example 8 of Zimmermann. As set forth above, appellants have not done so. On this record, it is reasonable to conclude that the same patient is being administered the same active agent by the same mode of administration in the same amount in both claim 1 on appeal and Example 8 of Zimmermann. The fact that appellants may have discovered yet another beneficial effect from the method set forth in Example 8 of Zimmermann does not mean that they are entitled to receive a patent on that method.

4. Rejection Under 35 U.S.C. § 102(f).

Our affirmance of the rejection under 35 U.S.C. § 102(e) constitutes a disposition of this appeal. Accordingly, we do not consider the merits of the examiner's alternative rejection under 35 U.S.C. § 102(f). The decision of the examiner is affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

William F. Smith)
Administrative Patent Judge)
)
)
Demetra J. Mills) BOARD OF PATENT
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)
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